

## **REMARKS**

### **Status of the Claims**

Claims 1-3, 6-13, 18-25, 28, 37 and 38 are currently pending in this application. In this amendment, claims 1, 6, 12, 37 and 38 are amended to clarify the invention and to correct a minor typographical error; and claim 13 is canceled without prejudice or disclaimer. Support for the amendment is found in the specification as filed at page 12, lines 16-17 and in original claim 13. Thus, no new matter has been added. Upon entry of the amendment, claims 1-3, 6-12, 18-25, 28, 37 and 38 will be pending and subject to further examination. Entry of the amendment and reconsideration on the merits in view of the following comments is respectfully requested.

With respect to all amendments, Applicants have not dedicated or abandoned any unclaimed subject matter and have not acquiesced to any rejections and/or objections made by the Patent Office. Applicants expressly reserve the right to pursue prosecution of any presently excluded subject matter or claim embodiments in one or more future continuation and/or divisional application(s).

### **Correction of Inventorship**

As mentioned in the previous Response, Applicants recently discovered a typographical error in the name of one of the inventors. Specifically, it was noted that the correct name of the inventor currently identified as **Jing CHEN** is **Jing CHENG**.

The Office alleges that the request to correct the inventorship of this nonprovisional application under 37 CFR 1.48(a) is deficient because: (1) an oath or declaration by each actual inventor or inventors listing the entire inventive entity has not been submitted; (2) a 37 CFR 3.73(b) submission has not been received to support action by the assignee; (3) it lacks the required fee under 37 CFR 1.17(i); and (4) the statement of facts by an inventor or inventors to be added or deleted does not explicitly state that the inventorship error occurred without deceptive intent on his or her part or cannot be construed to so state.

It is respectfully submitted that no petition, oath or declaration is required in this situation. As Applicants clearly stated in the previous response, the present inventorship error is purely typographical. No new inventors are being added, and no listed inventors are being deleted. MPEP § 201.03 expressly states: **“A request under 37 CFR 1.48 will not be required: (B) Where a typographical or transliteration error in the spelling of an inventor’s name is discovered, the Office should simply be notified of the error. A new oath or declaration is not required...** Reference to the notification will be made on the previously filed oath or declaration.” Similarly, MPEP § 605.04(b) expressly states: **“When a typographical or transliteration error in the spelling of an inventor’s name is discovered during pendency of an application, a petition is not required, nor is a new oath or declaration under 37 CFR 1.63 needed.”** In addition, a replacement Application Data Sheet (ADS) containing the correct spelling of all the inventors’ names was submitted on July 28, 2009. Accordingly, Applicants respectfully request that this formal objection may be withdrawn.

#### **Rejections under 35 U.S.C. § 103**

##### ***Dauer in View of Iinuma or O’Neill and Grevelding***

Claims 1-3, 6-9, 12-13, 18, 24-25, 28 and 37 are rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Dauer *et al.* (*Biotechnol. Bioeng.*, 37:1021-1028 (1991), hereinafter “Dauer”) in view of Iinuma *et al.* (*Int. J. Cancer* 2000, 89:337-344, hereinafter “Iinuma”) and Grevelding *et al.* (*Nucleic Acids Res.*, 24(20):4100-4101 (1996), hereinafter “Grevelding”).

Claims 1-3, 6-9, 12-13, 18, 20-25, 28 and 38 are rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Dauer in view of O'Neill *et al.* (U.S. Patent 6,187,546, hereinafter “O’Neill”) and Grevelding.

Dauer allegedly teaches a method of isolating cells using magnetic particles. With regard to claim 1, Dauer allegedly teaches a process for amplifying a nucleic acid of a target cell or virus, which process comprises: a) contacting a sample containing or suspected of containing a target cell or virus with a magnetic microbead not comprising a biomolecule that binds to said target cell or

virus with high specificity (p. 1024, col. 2, where baker's yeast were the target cells and where the magnetic microbead comprises a magnetic "seed" comprising ferromagnetic gamma-iron oxide or maghemite ( $\text{Fe}_2\text{O}_3$ ); see Table 1); b) allowing said target cell or virus, if present in said sample, to bind to said magnetic microbead to form a conjugate between said target cell or virus and said magnetic microbead (Figure 6, where the process of mixing, binding and separation are depicted; p. 1025, col. 2, and where the pH is used to control binding to the particles and then release of the particles); c) separating said conjugate from other undesirable constituents via a magnetic force to isolate said target cell or virus from said sample (Figure 6E, where the conjugate between the magnetic particle and the cells are separated from the sample), wherein said biomolecule is selected from the group consisting of an antibody, an amino acid, a peptide, a protein, a nucleoside, a nucleotide, an oligonucleotide, a nucleic acid, a vitamin, a monosaccharide, an oligosaccharide, a carbohydrate, a lipid and a complex thereof (Table 1, p. 1024, col. 2, where the magnetic particle is not coated with a biomolecule or other affinity group).

The Office acknowledges that Dauer does not teach that the target cells can comprise leukocytes, as required by claims 1-3, 6-9, 12-13, 18, 24-25, 28 and 37. To cure this deficiency of Dauer, the Office cites Iinuma, which allegedly teaches that leukocytes can be specifically targeted by magnetic beads comprising anti-CD45 monoclonal antibodies (p. 337, col. 2).

Similarly, the Office acknowledges that Dauer does not teach that the target cells can comprise epithelial cells, as required by claims 1-3, 6-9, 12-13, 18, 24-25, 28 and 38. To cure this deficiency of Dauer, the Office cites O'Neill, which allegedly teaches a saliva sample containing or suspected of containing an epithelial cell (col. 20, where epithelial cells are exfoliated into saliva or sputum), wherein the epithelial cell is enriched and isolated by binding to a magnetic particle (col. 20, lines 32-35, where epithelial cells are enriched using magnetic particle sorting).

The Office further acknowledges that Dauer does not explicitly teach that the cells can be applied to an amplification system. To cure this deficiency of Dauer, the Office cites Grevelding, which allegedly teaches a method comprising d) applying said separated conjugate to a nucleic acid amplification system to amplify a nucleic acid from said target cell or virus, wherein said process

does not comprise a step of lysing said target cell or virus to release said nucleic acid prior to applying said separated conjugate to said nucleic acid amplification system (Abstract, p. 4100, col. 1, where the technique of PCR is applied to whole organisms and has been applied to yeast and bacteria).

The Office argues that it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have analyzed the target cells of *Linum* using the method of separation taught by Dauer to arrive at the claimed invention with a reasonable expectation for success. *Linum* allegedly teaches that “prepared cells were resuspended in 80  $\mu$ l of BSA-PBS mixed with 20  $\mu$ l of CD45 microbeads for 15 min at 4°C and passed down the MACS column” (p. 338, col. 1). Therefore, the Office argues that one of ordinary skill in the art at the time the invention was made would have been motivated to have analyzed the target cells of *Linum* using the method of separation taught by Dauer to arrive at the claimed invention with a reasonable expectation for success.

Furthermore, the Office argues that it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have adjusted the method of Dauer to include further analysis of the captured and released cells using PCR amplification as taught by Grevelding to arrive at the claimed invention with a reasonable expectation for success. Grevelding allegedly teaches that “recently protocols were introduced that allow PCR amplification without DNA extraction” and that “PCR amplification is possible from whole, undissected larvae and adults of the fruitfly *Drosophila melanogaster* and the blood fluke, *Schistosoma mansoni* without preceding DNA isolation.” Regarding the applicability of the method to other types of cells, Grevelding allegedly teaches that “[s]ince it worked both with an organism covered by a tegument as well as one surrounded by a chitinous cuticle, it is expected that it should also be applicable for a variety of other eukaryotic organisms” (p. 4101, col. 1). The Office takes the position that while Grevelding teaches isolation from whole organisms, the technique of amplification directly from cells without prior DNA extraction is clearly supported by the teachings of Grevelding. Therefore, the Office argues that one of ordinary skill in the art would have been motivated to have adjusted the method of Dauer to include further analysis of the captured and released cells using PCR

amplification as taught by Grevelding to arrive at the claimed invention with a reasonable expectation for success.

As an initial matter, claim 13 has been canceled, and claims 1, 37 and 38 have been amended to specify that the magnetic microbead is modified to comprise a hydroxyl, a carboxyl or an epoxy group. As noted above, support for the amendment is found in the specification as filed at page 12, lines 16-17 and in original claim 13. Since each of claims 2, 3, 6-9, 12, 18, 24-25 and 28 depends, directly or indirectly, from claim 1, these claims incorporate the new limitations of claim 1 as well. With respect to claims 1-3, 6-9, 12, 18, 24-25, 28, 37 and 38, Applicants respectfully traverse these rejections for the reasons set forth below.

The obviousness analysis under 35 U.S.C. § 103(a) requires the consideration of the scope and content of the prior art, the level of skill in the relevant art, and the differences between the prior art and the claimed subject matter must be considered. *KSR Int'l Co. v. Teleflex Inc.*, 127 S.Ct. 1727 (2007) (citing *Graham v. John Deere Co.*, 383 U.S. 1, 17 (1966)). Rejections on obviousness grounds cannot be sustained by mere conclusory statements. *In re Kahn*, 441 F.3d 977, 987-88 (Fed. Cir. 2007) (citations omitted). Critical elements of the invention as a whole which clearly distinguish the entire invention from the prior art references cannot be ignored. *Panduit Corp. v. Dennison Manufacturing Co.*, 1 U.S.P.Q.2d 1593, 1597 (Fed. Cir.), *cert. denied*, 481 U.S. 1052 (1987). Evidence of an unobvious or unexpected advantageous property can rebut *prima facie* obviousness. MPEP § 716.02(a).

Dauer teaches the use of high gradient magnetic separation (HGMS) to separate nonmagnetic microorganisms such as the baker's yeast (*Saccharomyces cerevisiae*) from solution by a technique known as seeding, whereby fine magnetic particles are adhered to the cells' surfaces, making them magnetic and amenable to magnetic separation. (See Abstract). Dauer further teaches that technique may be used to recover microorganisms from dilute process streams and is particularly well suited to the final clean-up and isolation of proprietary or hazardous organisms. (See Dauer at page 1027, right col.) Thus, Dauer is primarily concerned with large-scale magnetic separation of microorganisms from solution.

Iinuma teaches highly specific separation of CD45<sup>+</sup> cells using magnetic microbeads coated with anti-CD45 antibodies (page 338, emphasis added). Similarly, O'Neill teaches highly specific separation of exfoliated cells in sputum or saliva using magnetic beads coated with Ber-EP4 antibody specific for epithelial cells (col. 20, lines 32-35). Neither Iinuma nor O'Neill teaches or even suggests nonspecific or low-specificity magnetic separation of mammalian cells, particularly leukocytes or epithelial cells.

Grevelding teaches that direct DNA amplification by PCR may be performed on fruitflies and blood flukes without DNA purification. Grevelding also teaches that similar protocols had been developed for microorganisms such as protozoans, bacteria and yeast. (See Grevelding at page 4100, left col.) Grevelding does not contain any discussion regarding magnetic separation at all.

The obviousness analysis requires the consideration of the differences between the claimed invention "as a whole" and the prior art. Thus, here it is critical to understand the difference between the claimed invention "as a whole" and the inventions of the cited references, namely, Dauer, Iinuma or O'Neill and Grevelding, "as a whole".

As an initial matter, none of the cited references teaches or even suggests nonspecific or low-specificity magnetic separation of mammalian cells, particularly leukocytes or epithelial cells, using magnetic microbeads modified to comprise a hydroxyl, a carboxyl or an epoxy group. Moreover, none of the cited references provides any indication that direct PCR amplification would be effective on mammalian cells, particularly leukocytes or epithelial cells.

As discussed previously, the present invention stems from the surprising observation that magnetic beads that do not bind to a target cell with high specificity can nevertheless be used successfully to isolate leukocytes from a whole blood sample or epithelial cells from a saliva sample to such an extent that these cells may be subjected to nucleic acid amplification (e.g., PCR of the HLA-A gene for HLA typing) without having to elute the nucleic acid from the magnetic beads.

Whole blood is a complex mixture of cells (e.g., leukocytes, erythrocytes and platelets), proteins, lipids, carbohydrates and other low-molecular weight compounds, many of which tend to

affect the accuracy of analytical methods to various extents. The ratio of leukocytes to erythrocytes, which lack nucleic acids, is approximately 1/1000. Even 1% of whole blood in a sample can effectively inhibit a nucleic acid amplification reaction, which is believed to be due to the binding of heme to DNA polymerase. Thus, isolation of leukocytes from whole blood is critical for nucleic acid amplification. Conventional centrifugation techniques for separating leukocytes are labor-intensive and time consuming. Most commercially available methods at the time of the invention involved the use of CD45 antibody-coated magnetic particles (*see, e.g.,* Jinuma), which are not suitable for routine use due to the high price and biological instability of antibody-coated beads.

The present inventors discovered that leukocytes could be successfully separated from the other components in whole blood by using magnetic particles modified with organic molecules such as carboxyl, hydroxyl or epoxy groups, even in the absence of specific interactions between the magnetic particles and leukocytes. (*See, e.g.,* Example 1.) Consequently, interfering contaminants in the whole blood, such as erythrocytes and proteins, could be largely eliminated. (*See, e.g.,* Fig. 1, lanes 3 and 4.) This discovery was contrary to the conventional practice of using immunomagnetic particles for the separation of leukocytes from whole blood and could not have been reasonably anticipated based on the disclosure of the cited prior art references. Additionally, it was surprisingly found that the leukocyte-magnetic particle complex could be used as a template for nucleic acid amplification without nucleic acid elution, which allows integrating the separation and amplification steps into a single, easy-to-automate process.

Much like whole blood, saliva is also a complex mixture of cells (*e.g.,* epithelial cells), electrolytes, mucus, antibacterial compounds and various protein enzymes. Because saliva is fairly abundant and convenient to collect, saliva samples have been used for DNA-based diagnostics for a while. However, since saliva contains a number of substances that may interfere with nucleic acid amplification, separation of nucleated cells prior to amplification is desirable. Historically, such separation has been accomplished by centrifugation, which is somewhat difficult to miniaturize. Immunomagnetic separation of epithelial cells from saliva samples has also been used, but it suffers from the same shortcomings as discussed above in the context of leukocytes and whole blood.

The present inventors discovered that epithelial cells could be successfully isolated from the other components in saliva by using magnetic particles modified with organic molecules such as carboxyl, hydroxyl or epoxy groups, even in the absence of specific interactions between the magnetic particles and epithelial cells. (See, e.g., Example 2.) Consequently, interfering components in the saliva could be significantly reduced to the point where they no longer prevent nucleic acid amplification. (See, e.g., Fig. 1, lanes 5 and 6.) Once again, this discovery was contrary to the conventional practice of using immunomagnetic particles for the separation of epithelial cells and could not have been reasonably expected based on the disclosure of the cited prior art references. Additionally, it was surprisingly found that the epithelial cell-magnetic particle conjugate could be used as a template for nucleic acid amplification without nucleic acid elution, which allows integrating the separation and amplification steps into a single, easy-to-automate process.

The Office's entire line of reasoning is scientifically flawed. The Office attempts to combine Dauer, which teaches non-specific separation of yeast cells, with Iinuma or O'Neill, both of which teach highly specific immunomagnetic separation of mammalian cells. However, as Applicants indicated previously, there was no motivation in the art to use non-specific magnetic separation for mammalian cells. In fact, the prior art taught away from magnetic beads that bind to cells non-specifically:

**Magnetic beads for use in cell separation should fulfil [sic] some important criteria, i.e., they should be chemically stable and should not aggregate in the media used in cell separation, they should show very little magnetic remanence after having been subjected to the magnetic field, they should not bind to cells non-specifically, there should be very little leakage of the immobilized affinity ligand (Ab, antigen, lectin, carbohydrate) from the particles during storage, they should allow a fast and complete magnetic separation of the cells labelled with particles and of excess particles from the unlabelled cells, and they should be of a size which minimizes phagocytosis. Majority of the commercially available particles fulfils these requirements.**

(Safarik & Safarikova, "Use of magnetic techniques for the isolation of cells," *J. Chromatogr. B*, 1999, 722: 33-53, attached herewith as *Exhibit A*, at page 36, right col., emphasis added.)



Moreover, the Office is ignoring critical structural distinctions between yeast and mammalian cells. It was well known in the art at the time of the invention that yeast cells are protected by a thick (100 to 200 nm) cell wall, which contains 15 to 30% of the dry mass of the cell. Major structural constituents of the cell wall are polysaccharides (80-90%), mainly glucans and mannans, with a minor percentage of chitin. Glucans ( $\beta$ -1,3 and  $\beta$ -1,6) provide strength to the cell wall, forming a microfibrillar network. Mannans are present as an  $\alpha$ -1,6-linked inner core with  $\alpha$ -1,2 and  $\alpha$ -1,3 side chains. Chitin, an N-acetylglucosamine polymer, represents 2-4% of the cell wall and is located primarily in bud scars. Other components of the cell wall are variable quantities of proteins, lipids, and inorganic phosphate. For a review of yeast cell wall biology, see Lipke & Ovalle, "Cell Wall Architecture in Yeast: New Structure and New Challenges," *J. Bacteriol.*, 1998, 180: 3735-3740 (attached herewith as **Exhibit B**). In contrast, mammalian cells such as leukocytes and epithelial cells do not have a cell wall. The mammalian cell membrane is composed primarily of lipids, such as phospholipids, glycolipids and cholesterol, and the content of polysaccharides in a mammalian outer membrane layer is significantly lower than in the yeast cell wall. Accordingly, based on the disclosure of Dauer that non-specific magnetic separation was effective for large-scale yeast separation, a person skilled in the art at the time of the invention could not have reasonably expected that the same technique would have been successful in mammalian cells such as leukocytes or epithelial cells.

Thus, there is substantial evidence that a person skilled in the art at the time of the invention could not have been motivated to use the non-specific magnetic separation of yeast cells as taught in Dauer to separate mammalian cells, such as the leukocytes as taught in Iinuma or the epithelial cells as taught in O'Neill. There is also substantial evidence that a person skilled in the art at the time of the invention could not have had a reasonable expectation of success because the membranes of leukocytes and epithelial cells have a completely different chemical composition than yeast cells.

Because the combinations of Dauer, Iinuma and Greveling or Dauer, O'Neill and Greveling fail to teach all the limitations of claims 1, 37 and 38 as amended, and because there was no reasonable motivation to combine the teachings of Dauer with those of Iinuma or O'Neill and Greveling with a reasonable expectation of success, the Office has failed to establish a *prima facie*

case of obviousness. Accordingly, it is respectfully submitted that these rejections under 35 U.S.C. § 103(a) may properly be withdrawn.

***Dauer in View of Iinuma and Grevelding and Further in View of Lopez-Sabater***

Claims 5 and 29 are rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Dauer in view of Iinuma and Grevelding as applied to claims 1-3, 6-9, 12-13, 18, 20-25, 28 and 37 above, and further in view of Lopez-Sabater *et al.* (*Lett. Appl. Microbiol.*, 24:101-104 (1997), hereinafter “Lopez-Sabater”).

As noted in the previous Response, this rejection is moot in view of the earlier cancellations of claims 5 and 29.

***Dauer in View of Iinuma and Grevelding and Further in View of Ughelstad***

Claim 10 is rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Dauer in view of Iinuma and Grevelding as applied to claims 1-3, 6-9, 12-13, 18, 20-25, 28 and 37 above, and further in view of Ughelstad *et al.* (WO 83/103920 (1983), hereinafter “Ughelstad”).

The Office acknowledges that Dauer does not explicitly teach that the magnetic beads can be made of  $\text{Fe}_3\text{O}_4$ . To cure this deficiency of Dauer, the Office cites Ughelstad, which allegedly teaches magnetic beads for use in separation wherein the metal composition is  $\text{Fe}_3\text{O}_4$ .

The Office argues that it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have applied the specific teachings of Ughelstad to the particles of Dauer to arrive at the claimed invention with a reasonable expectation for success. Dauer allegedly states: “The magnetic seed is a ferromagnetic  $\gamma$ -iron oxide ( $\gamma\text{-Fe}_2\text{O}_3$ ) or maghemite” (p. 1024, col. 2). Ughelstad teaches wherein the method composition comprises  $\text{Fe}_3\text{O}_4$  specifically (see p. 9). Therefore, the Office argues that one of ordinary skill in the art at the time the invention was made would have been motivated to have applied the specific teachings of Ughelstad to the particles of Dauer to arrive at the claimed invention with a reasonable expectation for success.

As noted above, claim 1 has been amended to specify that the magnetic microbead is modified to comprise a hydroxyl, a carboxyl or an epoxy group. Since claim 10 indirectly depends from claim 1, claim 10 incorporates the new limitation of claim 1 as well.

The teachings of Dauer, Iinuma and Greveling have been briefly discussed above. Ughelstad teaches various magnetic polymer particles prepared by treating compact or porous polymer particles with a solution of iron salts and, optionally, salts of other metals which are capable of forming magnetic ferrites, in which the solution swells or penetrates into the particles.

Ughelstad fails to provide any teachings that would cure the deficiencies of Dauer, Iinuma and Greveling as discussed above. Much like Dauer, Iinuma and Greveling, Ughelstad does not teach or suggest nonspecific or low-specificity separation of mammalian cells, particularly leukocytes or epithelial cells, using magnetic microbeads modified to comprise a hydroxyl, a carboxyl or an epoxy group. Moreover, much like Dauer, Iinuma and Greveling, Ughelstad does not provide any indication that direct PCR amplification would be effective on mammalian cells, particularly leukocytes or epithelial cells. Since the combination of Dauer, Iinuma, Greveling and Ughelstad fails to teach several important elements of claim 10 as amended herein, the Office has failed to establish a *prima facie* case of obviousness. Accordingly, it is respectfully submitted that this rejection under 35 U.S.C. § 103(a) may properly be withdrawn.

#### ***Dauer in View of Greveling and Further in View of Dzieglewska***

Claims 11 and 19 are rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Dauer in view of O'Neill and Greveling as applied to claims 1-3, 6-9, 12-13, 18, 20-25, 28 and 38 above, and further in view of Dzieglewska (WO 98/51693 (1998), hereinafter "Dzieglewska").

The Office acknowledges that Dauer does not explicitly teach the additional limitations of claims 11 and 19. To cure these deficiencies of Dauer, the Office cites Dzieglewska, which allegedly teaches magnetic microbead having a diameter ranging from about 5 to about 50,000 nanometers (claim 11); an automated method of nucleic acid isolation (claim 19); and a target cell comprising a bacteria or eukaryotic cell and can be obtained from a urine sample).

The Office argues that it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have adjusted the teachings of Dauer to the include elements of Dzieglewska to arrive at the claimed invention with a reasonable expectation for success. Although the Office acknowledges that Dzieglewska teaches a method comprising lysis of cells prior to amplification, the Office argues that the elements of the claims represented by Dzieglewska are obvious in combination with the teaching of Dauer, O'Neill and Grevelding. Accordingly, the Office concludes that one of ordinary skill in the art at the time the invention was made would have been motivated to have adjusted the teachings of Dauer, O'Neill and Grevelding to the include elements of Dzieglewska to arrive at the claimed invention with a reasonable expectation for success.

As noted above, claim 1 has been amended to specify that the magnetic microbead is modified to comprise a hydroxyl, a carboxyl or an epoxy group. Since claims 11 and 19 directly depend from claim 1, both of these claims incorporate the new limitation of claim 1 as well.

The teachings of Dauer, O'Neill and Grevelding have been briefly discussed above. A careful review of Dzieglewska reveals that it fails to provide any teachings that would cure the deficiencies of Dauer, O'Neill and Grevelding as discussed above. For example, Dzieglewska does not teach or suggest a magnetic microbead is modified to comprise a hydroxyl, a carboxyl or an epoxy group. Further, much like Dauer, O'Neill and Grevelding, Dzieglewska does not teach or suggest nonspecific or low-specificity magnetic separation of mammalian cells, particularly leukocytes or epithelial cells. Moreover, much like Dauer, O'Neill and Grevelding, Dzieglewska does not provide any indication that direct PCR amplification would be effective on mammalian cells, particularly leukocytes or epithelial cells. Since the combination of Dauer, O'Neill, Grevelding and Dzieglewska fails to teach several important elements of claims 11 and 19 as amended herein, the Office has failed to establish a *prima facie* case of obviousness. Accordingly, it is respectfully submitted that this rejection under 35 U.S.C. § 103(a) may properly be withdrawn.

**CONCLUSION**

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing **docket No. 514572000700**. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

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Respectfully submitted,

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